Paper No. 14

UNITED STATES PATENT AND TRADEMARK OFFICE

BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES

Ex parte CAROL L. MacLEOD

Appeal No. 2001-1651
Application No. 09/238,972

ON BRIEF

Before ADAMS, MILLS and GRIMES, Administrative Patent Judges.

ADAMS, Administrative Patent Judge.

DECISION ON APPEAL

This is a decision on the appeal under 35 U.S.C. § 134 from the examiner's final rejection of claims 1-9, 16 and 17. As a result of a Restriction Requirement, the only remaining claims, claim 10-15 and 18-20, have been withdrawn from consideration, as drawn to a non-elected invention.

Claim 1, 3 and 16 are illustrative of the subject matter on appeal and are reproduced below:

1. A method of inhibiting cationic amino acid transport comprising the step of administering to a human or a non-human mammal an effective dose of an antisense oligonucleotide directed against CAT2 mRNA.

3. A pharmaceutical composition comprising an antisense oligonucleotide directed against CAT2 mRNA and a physiologically acceptable carrier.

16. An antisense oligonucleotide directed against CAT2 mRNA.

The references relied upon by the examiner are:

MacLeod	5,312,733	May 17, 1994
Hoke et al. (Hoke)	5,585,479	Dec. 17, 1996

Gewirtz et al. (Gewirtz), "Facilitating oligonucleotide delivery: Helping antisense deliver on its promise," Proc. Natl. Acad. Sci. USA, Vol. 93, pp. 3161-63 (1996)

Rojanasakul, "Antisense oligonucleotide therapeutics: drug delivery and targeting," Advanced Drug Delivery Reviews, Vol. 18, pp. 115-31 (1996)

Branch, "A good antisense molecule is hard to find," TIBS, Vol. 23, pp. 45-50 (1998)

GROUNDS OF REJECTION

Claims 3 and 16 stand rejected under 35 U.S.C. § 112, first paragraph, as the specification that fails to adequately describe the claimed invention.

Claims 1-9 and 16 stand rejected under 35 U.S.C. § 112, first paragraph, as being based on an insufficient disclosure to support or enable the scope of the claimed invention.

Claims 3, 16 and 17 stand rejected under 35 U.S.C. § 102(b) as being anticipated by MacLeod.

We affirm the rejection under 35 U.S.C. § 102(b) and reverse the rejections under 35 U.S.C. § 112, first paragraph.

DISCUSSION

THE REJECTIONS UNDER 35 U.S.C. § 112, FIRST PARAGRAPH:

Written Description:

"In order to satisfy the written description requirement, the disclosure as originally filed does not have to provide in haec verba support for the claimed

subject matter at issue." Purdue Pharma L.P. v. Faulding, Inc., 230 F.3d 1320, 1323, 56 USPQ2d 1481, 1483 (Fed. Cir. 2000). Nonetheless, the disclosure must convey with reasonable clarity to those skilled in the art that the inventor was in possession of the invention. See id. "Put another way, one skilled in the art, reading the original disclosure, must immediately discern the limitation at issue in the claims." Id.

According to the examiner, (Answer, page 4), claims 3 and 16 are "drawn to any antisense oligo which inhibits CAT2 translation and pharmaceutical compositions comprising said antisense oligo." Based on this interpretation of the claims, the examiner finds (id.) that while the specification describes the inhibitory activity of an antisense oligo consisting of SEQ ID NO: 2, the specification fails to describe any other antisense oligo, or pharmaceutical composition comprising such an antisense oligo, that exhibited inhibitory activity. However, in response, appellant points out that the entire sequence of the CAT2 open reading frame was set forth in "MacLeod et al. Mol. Cell. Biol., 10:3663-3674 (1990) and is also available from GenBank as accession no. M32485," and that with knowledge of the open reading frame "one skilled in the art could easily design other effective antisense oligonucleotides." Brief, page 12.

As set forth in Moba B.V. v. Diamond Automation Inc., 325 F.3d, 1306, 1320-21, 66 USPQ2d 1429, 1439 (Fed. Cir. 2003):

> The test for compliance with § 112 has always required sufficient information in the original disclosure to show that the inventor possessed the invention at the time of the original filing. See ... [Vas-Cath Inc. v. Mahurkar, 935 F.2d 1555, 1561, 19 USPQ2d 1111, 1115 (Fed. Cir. 1991)] ("Adequate description of the

> invention guards against the inventor's overreaching by insisting that he recount his invention in such detail that his future claims can be determined to be encompassed within his original creation"). The possession test requires assessment from the viewpoint of one of skill in the art. Id. at 1563-64 ("the applicant must ... convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention") (emphasis in original); Union Oil Co. of Cal. v. Atlantic Richfield Co., 208 F.3d 989, 997, 54 USPQ2d 1227, 1232 (Fed. Cir. 2000) ("The written description requirement does not require the applicant 'to describe exactly the subject matter claimed, [instead] the description must clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed'") (citation omitted). In Enzo [Biochem, Inc. v. Gen-Probe, Inc., 296 F.3d 1316, 63 USPQ2d 1609 (Fed. Cir. 2002)] and Amgen[Inc. v. Hoechst Marion Roussel Inc., 314 F.3d 1313, 1330, 65 USPQ2d 1385, 1397 (Fed. Cir. 2003)], the record showed that the specification that taught one of skill in the art to make and use an invention also convinced that artisan that the inventor possessed the invention. Similarly in this case, the Lilly [Regents of the University of California v. Eli Lilly & Co., 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997)] disclosure rule does not require a particular form of disclosure because one of skill could determine from the specification that the inventor possessed the invention at the time of filing.

On this record, the examiner bases his rejection on an incorrect interpretation of the claimed invention. Contrary to the examiner's assertion (Answer, page 4), claims 3 and 16 do not require the inhibition of CAT2 translation. Instead, claim 16 is drawn to an antisense oligonucleotide directed against CAT2 mRNA, and claim 3 is drawn to a composition comprising an antisense oligonucleotide directed against CAT2 mRNA in a physiologically acceptable carrier. We note that while a number of appellant's claims are directed at methods of using an antisense CAT2 oligonucleotide, none of these claims are included in this rejection.

In addition, the examiner failed to consider the level of skill in the art as it relates to the claimed invention. To the contrary, by incorrectly interpreting the claimed invention to require the claimed antisense oligonucleotide, or a pharmaceutical composition thereof, to have the ability to inhibit CAT2 mRNA translation the examiner created an artificial claim. The examiner then attacks this artificial claim finding no written descriptive support in the disclosure for an "antisense oligo that is capable of inhibiting CAT2 RNA thereby disrupting translation of cationic amino acid transport protein ... [or for] pharmaceutical compositions comprising the antisense oligo since no evidence is provided demonstrating the ameliorative effects of treatment with said antisense oligo." See Answer, page 5. These arguments, however, do not address the invention of claims 3 and 16.

Accordingly, it is our opinion that the examiner failed to provide the evidence necessary to establish that one of skill in the art could not determine from the specification that the inventor possessed the invention of claims 3 and 16 at the time of filing. Accordingly, we reverse the rejection of claims 3 and 16 under 35 U.S.C. § 112, first paragraph.

Enablement:

The initial burden of providing reasons why a supporting disclosure does not enable the claims rests with the examiner. In re Marzocchi, 439 F.2d 220, 223, 169 USPQ 367, 369 (CCPA 1971). It is the examiner's burden to establish that appellant's specification does not provide a sufficient disclosure, either through illustrative examples or terminology, for one skilled in the art to practice

the invention as broadly as claimed without having to resort to undue experimentation. See In re Vaeck, 947 F.2d 488, 496, 20 USPQ2d 1438, 1445 (Fed. Cir. 1991). In considering this issue, we note that appellant is not required to disclose every parameter encompassed by the claims. See In re Angstadt, 537 F.2d 498, 503, 190 USPQ 214, 218 (CCPA 1976). Furthermore, while some experimentation may be necessary, that does not preclude enablement; what is required is that the amount of experimentation "must not be unduly extensive." Atlas Powder Co. v. E.I. DuPont de Nemours & Co., 750 F.2d 1569, 1576, 224 USOQ 409, 413 (Fed. Cir. 1984).

On this record, the examiner finds (Answer, page 5),

> the specification is only enabling for claims limited to an antisense oligo consisting of SEQ ID NO:2 and a method of inhibiting CAT2 expression using said antisense oligo. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with ... [claims 1-9 and 16].

According to the examiner (Answer, page 6), "[a]lthough the specification provides guidance on a singular antisense oligo (SEQ ID NO: 2), it is well known by those skilled in the art that identification of target sites in a given mRNA at which antisense oligos bind to cause inhibition of translation is an unpredictable art."

With reference to Hoke, the examiner finds (Answer, page 7) that screening

> different sites on a given mRNA to find oligo binding sites for inhibition of translation, may fail to identify such sites in the 5' untranslated region, the coding region, or in the 3' untranslated region of the mRNA and that an oligo binding site that is located

> only a few bases to either side of an unsuccessful target site may give very effective inhibition of translation.

However, as appellant points out (Brief, page 15), Hoke report a 55% success rate in obtaining effective anti-sense oligonucleotides. According to appellant there is no reason why a similar success rate would not be expected for the instant invention. In response, the examiner backs away from his reliance on Hoke and agrees with appellant that Hoke reports a 55% success rate. Answer, page 10. Nevertheless, the examiner maintains that the instant invention would not be successful due to the unpredictability of antisense oligonucleotide therapy and target accessibility as taught by Gewirtz and Branch. Answer, bridging sentence, pages 10-11.

According to the examiner (Answer, page 7), Gewirtz "teach that the inhibitory activity of an oligo depends unpredictably on both the sequence and structure of the nucleic acid target site and the ability of the oligo to reach its target." Similarly, the examiner relies on Branch to teach that "'internal structures of target RNAs and their associations with cellular proteins create physical barriers, which render most potential binding sites inaccessible to antisense molecules.'" While the examiner argues that Gewirtz and Branch address the unpredictability of antisense technology, the examiner fails to establish a nexus between these generic references and the claims on appeal.

In addition, we find the examiner's position to be inconsistent. According to the examiner the specification provides an enabling disclosure of a method of inhibiting CAT2 expression using an antisense oligo consisting of SEQ ID NO:2.

Answer, page 5. We note that the examiner does not limit the scope of this method to exclude antisense oligonucleotide therapy. The only reasonable conclusion that can be drawn from the examiner's argument is that despite the teachings of Hoke, Gewirtz, and Branch an antisense oligo consisting of SEQ ID NO:2 can be used in an antisense oligonucleotide therapy method for inhibiting CAT2 expression. Thus, the generic teachings of Hoke, Gewirtz and Branch are not applicable to appellant's claimed methods.

According to appellant's specification (page 27), "[t]he present invention describes how novel antisense oligonucleotides can be employed to prevent cationic amino acid transport, which in turn blocks production of nitric oxide in cells such as activated macrophages or cancer cells." Appellant's specification discloses (page 28), "the present invention makes available novel antisense oligonucleotides for use in gene therapy where it may be desirable to inhibit production of nitric oxide." In the paragraph bridging pages 28-29, appellant's specification discloses that

> this method will treat diseases selected from the group consisting of sepsis, cachexia, neoplastic diseases such as Kaposi's sarcoma, cerebral malaria, capillary leak syndrome and autoimmune disease. Representative autoimmune diseases include systemic lupus erythematosus, rheumatoid arthritis and multiple sclerosis. Representative neoplastic diseases include breast and lung cancer.

The examiner recognizes (Answer, page 6), appellant's "specification teaches that CAT2 is involved in arginine transport which was shown to be essential in nitric oxide synthesis. In addition, iNOS expression was shown to be correlative with mammary tumorigenesis since mice with a functional iNOS gene

developed mammary tumors more rapidly than iNOS knockout mice." The examiner also finds (Answer, page 5), appellant's specification enables a method of inhibiting CAT2 expression using an antisense oligo consisting of SEQ ID NO:2. Therefore, it is unclear on this record, why the examiner finds (Answer, page 6) that appellant's "specification does not provide any guidance regarding the administration of any type [of] antisense oligo targeted to CAT2 that would result in an ameliorative effect of any particular pathological state nor does the specification provide sufficient guidance that would enable a skilled artisan to treat a pathological condition by inhibiting CAT2." As emphasized above, it seems clear from appellant's specification that inhibiting CAT2 expression, using an antisense oligo, will inhibit production of nitric oxide. Accordingly, it appears from this record that such a method would be applicable to the diseases set forth in appellant's specification. The examiner offers no evidence to the contrary.

Furthermore, since appellant's specification provides an enabling disclosure of an antisense oligo consisting of SEQ ID NO: 2 and a method of inhibiting CAT2 expression using this oligo, why would it require undue experimentation to identify other antisense CAT2 oligonucleotides with a success rate similar to that of Hoke? The examiner conceded the success rate observed by Hoke, and that appellant's oligonucleotide having SEQ ID NO.: 2 is effective in a method of inhibiting CAT2 expression. In view of these findings, the examiner failed to provide any explanation as to how the generic teachings of Gewirtz, and Branch apply to appellant's claimed invention. Stated differently,

the examiner failed to provide the evidence necessary to establish that appellant's specification does not support appellant's claimed invention.

To emphasize the inconsistent approach taken by the examiner, we note that claim 17 is drawn to an antisense CAT2 oligonucleotide having the sequence set forth in SEQ. ID. NO.: 2; and claim 2 is drawn to a method of using an antisense CAT2 oligonucleotide having the sequence set forth in SEQ. ID. NO.: 2. Notwithstanding the examiner's finding that the specification enables a method of inhibiting CAT2 expression using an antisense oligonucleotide consisting of SEQ ID NO.: 2, the examiner excludes claim 17 from the rejection, but includes claim 2 in the rejection.

In addition, we recognize the examiner's reliance on Rojanasakul (Answer page 7), which according to the examiner "gives evidence that the use of antisense oligonucleotides in vivo caused renal failure due to toxicity of the antisense oligonucleotide which could be due to nonspecific effects of the oligo itself...." The examiner, however, appears to confuse the requirements under the law for obtaining a patent with the requirements for obtaining government approval to market a particular drug for human consumption. See Scott v. Finney, 34 F.3d 1058, 1063, 32 USPQ2d 1115, 1120 (Fed. Cir. 1994) ("Testing for the full safety and effectiveness of a prosthetic device is more properly left to the Food and Drug Administration (FDA). Title 35 does not demand that such human testing occur within the confines of Patent and Trademark Office (PTO) proceedings").

Furthermore, to the extent that Rojanasakul may be relevant to the issue of patentability, we note that Rojanasakul (page 118, carry over paragraph, columns 1 and 2), report that thrombocytopenia and renal failure were induced by an antisense oligonucleotide targeted against the rel A transcription factor. While, Rojanasakul suggest (id.) that oligonucleotides can have non-specific actions and may cause toxic side effects in vivo, the examiner supplies no evidence to demonstrate that a person of ordinary skill in the art would reasonably expect the claimed antisense oligonucleotides to exhibit similar non-specific actions. In our opinion, the examiner failed to provide the evidence necessary to establish that appellant's specification does not support appellant's claimed invention.

As set forth in In re Armbruster, 512 F.2d 676, 677-78, 185 USPQ 152, 153 (CCPA 1975), quoting In re Marzocchi, 439 F.2d 220, 224, 169 USPQ 367, 369-70 (CCPA 1971):

> [I]t is incumbent upon the Patent Office, whenever a rejection on this basis [lack of enablement] is made, to explain why it doubts the truth or accuracy of any statement in a supporting disclosure and to back up assertions of its own with acceptable evidence or reasoning which is inconsistent with the contested statement.

For the foregoing reasons, it is our opinion that the examiner failed to provide the evidence necessary to support his position that appellant's disclosure does not support the full scope of the claimed invention. Accordingly, we reverse the rejection of claims 1-9 and 16 under 35 U.S.C. § 112, first paragraph, as being based on an insufficient disclosure to support or enable the scope of the claimed invention.

THE REJECTION UNDER 35 U.S.C. § 102:

As we understand appellant's claim grouping, claim 3 stands or falls alone, and claim 17 stands or falls together with claim 16. Brief, pages 6-7. Appellant, however, fails to separately argue the claims as required by 37 CFR § 1.192(c)(7) (1999). Accordingly, claims 3, 16 and 17 will stand or fall together. Since all claims stand or fall together, we limit our discussion to representative independent claim 16. 37 CFR § 1.192(c)(7) (1999).

According to the examiner (Answer, page 4), "MacLeod discloses the CAT2 cDNA double stranded sequence identified as SEQ ID NO: 5, ... and also discloses that antisense sequences can be used to inhibit CAT2 translation...." In response, appellant points out that the application involved in this appeal is a continuation-in-part of 08/187,634, which is a continuation-in-part of MacLeod. According to appellant, by reciting the continuity data on the first line of the specification in the instant application, the instant application properly incorporates by reference the earlier application. However, as set forth in In re De Seversky, 474 F.2d 671, 674, 164 USPQ 144, 146-47 (CCPA 1973):

> the statement that an application is a continuation-in-part, or a continuation, or a division, or in part a continuation of another application is in a broad sense a "reference" to the earlier application, but a mere reference to another application, or patent, or publication is not an incorporation of anything therein into the application containing such reference for the purposes of the disclosure required by 35 U.S.C. [§] 112. Likewise it does not serve to bring a disclosure within the requirements of 35 U.S.C. [§] 120 so as to give a later application the benefit of the filing date of an earlier application. The later application must itself contain the necessary disclosure. As we said in ... [In re Lund, 376 F.2d 982, 989, 153 USPQ 625, 631 (CCPA 1967)],

> As the expression itself implies, the purpose of "incorporation by reference" is to make one document become a part of another document by referring to the former in the latter in such a manner that it is apparent that the cited document is part of the referencing document as if it were fully set out therein. ...
>
> We held in Lund that the mere statement that an application is a "continuation-in-part" does not do that.

Accordingly, we are not persuaded by appellant's argument that simply reciting the continuing data on the first page of the specification incorporates the disclosure of the prior applications by reference.

We agree with appellant's argument (Brief, page 10), that a later filed application is entitled to the benefit of the filing date of an earlier filed application with regard to the subject matter that is common to both applications. However, as the examiner points out (Answer, page 9), "there was no common subject matter, particularly antisense oligos in application 08/187,634 [now U.S. Patent 5,866,123 ('123)], as noted by appellant[1], thereby barring applicants from priority benefit to ... [MacLeod] which was not copending with the current application."

Similar to the facts in this case, our appellate reviewing court explained in In re Chu, 66 F.3d 292, 297, 36 USPQ2d 1089, 1093 (Fed. Cir. 1995):

> It is elementary patent law that a patent application is entitled to the benefit of the filing date of an earlier filed application only if the disclosure of the earlier application provides support for the claims of the later application, as required by 35 U.S.C. Section 112. 35 U.S.C. Section 120. Mendenhall v. Cedarapids Inc., 5 F.3d 1557, 1566, 28 USPQ2d 1081, 1088-89 (Fed. Cir. 1993) ("A patentee cannot obtain the benefit of the filing date of an earlier application where the claims in issue could not have been made in the earlier application."), cert. denied, 114 S. Ct. 1540 (1994); see also Litton

[1] According to appellant (Brief, page 10), "U.S. Patent Application Ser. No. 08/187,634 does not discuss antisense oligonucleotides directed against CAT2 mRNA...."

> Sys., Inc. v. Whirlpool Corp., 728 F.2d 1423, 1438, 221 USPQ 97, 106 (Fed. Cir. 1984) (discussing filing dates of CIP applications). Thus, Chu is entitled to the benefit of the Doyle patent filing date only if the Doyle patent discloses the subject matter now claimed by Chu. This, however, is admitted by Chu not to be the case. In fact, Chu states that "the invention as now claimed[ ] was not described in the [Doyle] patent." ... Accordingly, Chu cannot obtain the benefit of the Doyle patent filing date for these claims and the Doyle patent was properly relied on as prior art.

Accordingly, in order for the instant application to be entitled under 35 U.S.C. § 120 to the filing date of an earlier application in the chain of applications it is part of, it must be shown that as to the inventions claimed there has been "continuing disclosure through the chain of applications, without hiatus." In re Schneider, 481 F.2d 1350, 1356, 179 USPQ 46, 50 (CCPA 1973). Accord In re Hogan, 559 F.2d 595, 609, 194 USPQ 527, 540 (CCPA 1977); In re Goodman, 476 F.2d 1365, 1368, 177 USPQ 574, 576 (CCPA 1973). Appellant admits on this record that the '123 patent "does not discuss antisense oligonucleotides directed against CAT2 mRNA...." Brief, page 10. Accordingly, there was no continuing disclosure through the chain of applications.

Appellant also argues (id.), "[g]iven the disclosure of the sequence [in the '123 patent], the design and selection of an antisense oligonucleotide against CAT2 mRNA was completely within range of one with ordinary skill in the art." However, as our appellate reviewing court held in Lockwood v. American Airlines, Inc., 107 F.3d 1565, 1572, 41 USPQ2d 1961, 1966 (Fed. Cir. 1997):

> While the meaning of terms, phrases, or diagrams in a disclosure is to be explained or interpreted from the vantage point of one skilled in the art, all the limitations must appear in the specification. The question is not whether a claimed invention is an obvious variant of that which is disclosed in the specification. Rather, a prior

> application itself must describe an invention, and do so in sufficient detail that one skilled in the art can clearly conclude that the inventor invented the claimed invention as of the filing date sought.

Accordingly, we do not agree with appellant's statement (Brief, page 10), "the specification of ... ['123] inherently provides the basis for support for antisense oligonucleotides directed against CAT2 mRNA since the specification discloses the gene sequence of CAT2."

For the foregoing reasons, we affirm the rejection of claim 16 under 35 U.S.C. § 102(b) as being anticipated by MacLeod. As set for above, claims 3 and 17 fall together with claim 16.

No time period for taking any subsequent action in connection with this appeal may be extended under 37 CFR § 1.136(a).

AFFIRMED-IN-PART

Donald E. Adams)
Administrative Patent Judge)
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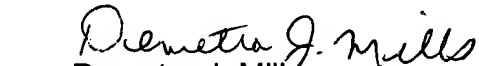
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